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EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1634

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/733,847	Applicant(s) CARR ET AL.	
	Examiner Frank W. Lu	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-30 is/are pending in the application.
- 4a) Of the above claim(s) 20,23-25 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-19,21,22,26,27,29 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of species (2) (claims 21, 22, and 26-28) and (6) (claims 22, 27, and 29) in the reply filed on March 26, 2007 is acknowledged. Therefore, claims 11-19, 21, 22, 26, 27, 29, and 30 will be examined.

Information Disclosure Statement

2. EP 13147783-A1 in the information disclosure statement filed on December 1, 2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

3. The disclosure is objected to because of the following informality: there are Figures 1A to 1F, 2A to 2G, 3A to 3D, 6A and 6B, 8A to 8C, 9A and 9B, 11A and 11B, 12A and 12B, 13A, and 13B, 14A and 14B, 15A to 15G, 16A to 16C, 20A and 20B, 21A and 21B, and 23A and 23B. However, BRIEF DESCRIPTION OF THE DRAWINGS only describes Figures 1-3, 6, 8, 9, 11-16, 20, 21, and 23.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. New Matter

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claim 18 requires that at least one component is cross-linked itself.

Although the specification describes crosslinking of mismatch recognition proteins to a pool of DNA sequences (e.g., see page 44, [0150]), paragraph 150 and Figure 17 of the specification suggested by applicant fails to define or provide any disclosure to support such claim recitation.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application".

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 17 is rejected as vague and indefinite because it is unclear that at least two components in the claim are the same or different from least one component in claim 14 or not. Please clarify.

9. Claim 18 is rejected as vague and indefinite because it is unclear that at least one component in the claim are the same or different from least one component in claim 14 or not. Please clarify.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 11-15, 19, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner, Jr. (US Patent No. 6,114,115, published on September 5, 2000).

Regarding claims 11-13, Wagner, Jr. teaches providing a plurality or pool of nucleic acid molecules synthesized to have a user-specified sequence and length and selectively amplifying error-free nucleic acid molecules from said plurality or pool, thereby decreasing the relative amount of any nucleic acid molecules that contain errors as recited in claim 11, providing a plurality or pool of nucleic acid molecules synthesized to have a user-specified sequence and

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length and correcting errors in said plurality or pool using nucleic acid molecules in said plurality or pool as a template for nucleic acid repair as recited in claim 12, and providing a plurality or pool of nucleic acid molecules synthesized to have a user-specified sequence and length and removing errors from portions of said nucleic acid molecules and recombining remaining portions of said nucleic acid molecules to yield nucleic acid molecules having an error-free sequence as recited in claim 13 (see column 9, lines 12-35 and columns 26 and 27).

Regarding claims 14, 15, and 19, Wagner, Jr. teaches further comprising the step of combining at least one error-containing nucleic acid molecule from said plurality or pool with at least one component (ie., mismatch binding proteins) that prevents amplification of the error-containing nucleic acid molecule as recited in claim 14 wherein the component is a mismatch binding protein as recited in claim 15 and the component (ie., mismatch binding proteins) comprises more than one molecule (ie., more than one identical molecule) as recited in claim 19 (see column 9, lines 12-35 and columns 26 and 27).

Regarding claim 30, since the nucleic acid molecules in the plurality or pool with errors are used in the assay taught by Wagner, Jr. (see column 9, lines 12-35 and columns 26 and 27), Wagner, Jr. discloses that no nucleic acid molecules in the plurality or pool need be error-free as recited in claim 30.

Therefore, Wagner, Jr. teaches all limitations recited in claims 11-15, 19, and 30.

12. Claims 11-15, 19, 21, 22, 26, 27, 29, and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Modrich *et al.*, (US Patent No. 5,922,539, published on July 13, 1999).

Regarding claims 11-13, Modrich *et al.*, teach providing a plurality or pool of nucleic

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acid molecules synthesized to have a user-specified sequence and length and selectively amplifying error-free nucleic acid molecules from said plurality or pool, thereby decreasing the relative amount of any nucleic acid molecules that contain errors as recited in claim 11, providing a plurality or pool of nucleic acid molecules synthesized to have a user-specified sequence and length and correcting errors in said plurality or pool using nucleic acid molecules in said plurality or pool as a template for nucleic acid repair as recited in claim 12, and providing a plurality or pool of nucleic acid molecules synthesized to have a user-specified sequence and length and removing errors from portions of said nucleic acid molecules and recombining remaining portions of said nucleic acid molecules to yield nucleic acid molecules having an error-free sequence as recited in claim 13 (see column 2, lines 24-65, column 7, lines 55-67, column 8, lines 1-3, column 22, claim 10, and Figures 1 and 2).

Regarding claims 14, 15, and 19, Modrich *et al.*, teach further comprising the step of combining at least one error-containing nucleic acid molecule from said plurality or pool with at least one component (ie., mismatch binding protein such as MutS and MutH) that prevents amplification of the error-containing nucleic acid molecule as recited in claim 14 wherein the component is a mismatch binding protein (ie., MutS) as recited in claim 15 and the component (ie., mismatch binding protein such as MutS) comprises more than one molecule (ie., more than one identical molecule) as recited in claim 19 (see column 3, lines 51-65 and column 5, lines 22-30).

Regarding claims 21, 22, 26, 27, and 29, Modrich *et al.*, teach the step of correcting errors comprising the step of mismatch recognition and cleavage as recited in claim 21 wherein the step of mismatch recognition and cleavage is performed by a combination of a mismatch

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binding protein (ie., MutS) and a nuclease (ie., MutH) as recited in claim 22, the step of removing errors comprising the step of mismatch recognition and cleavage as recited in claim 23 wherein the step of mismatch recognition and cleavage is performed by a combination of a mismatch binding protein (ie., MutS) and a nuclease (ie., MutH) as recited in claim 27 and the step of removing errors is performed by the separate action of a mismatch binding protein (ie., MutS) and a nuclease (ie., MutH) as recited in claim 29 (see column 2, lines 24-65, column 3, lines 51-65, column 5, lines 22-30, column 7, lines 55-67, column 8, lines 1-3, and column 22, claim 10).

Regarding claim 30, since the nucleic acid molecules in the plurality or pool with errors are used in the assay taught by Modrich *et al.*, (see column 2, lines 24-65, column 7, lines 55-67, column 8, lines 1-3, column 22, claim 10, and Figures 1 and 2)), Modrich *et al.*, disclose that no nucleic acid molecules in the plurality or pool need be error-free as recited in claim 30.

Therefore, Modrich *et al.*, teach all limitations recited in claims 11-15, 19, 21, 22, 26, 27, 29, and 30.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Modrich *et al.*, as applied to claims 11-15, 19, 21, 22, 26, 27, 29, and 30 above, and further in view of Makrigiorgos (US Patent No. 7,033,757 B2, filed on May 15, 2001).

The teachings of Modrich *et al.*, have been summarized previously, *supra*.

Modrich *et al.*, do not disclose that the component is cross-linked to the error-containing nucleic acid molecule as recited in claim 16 wherein at least two components are cross-linked to each other as recited in claim 17.

Makrigiorgos teaches that the component (ie., MutY) is cross-linked to the error containing nucleic acid molecule as recited in claim 16 wherein at least two components (ie., MutY and the error containing nucleic acid molecule) are cross-linked to each other as recited in claim 17 (see columns 14, 15, and 28).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 16 and 17 wherein the component (ie., MutH) is cross-linked to the error-containing nucleic acid molecule and at least two components are cross-linked to each other in view of prior art of Modrich *et al.*, and Makrigiorgos. One having ordinary skill in the art would have been motivated to do so because Makrigiorgos suggests that crosslinking of mismatch repair enzyme (ie., MutY) to an

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error-containing nucleic acid molecule would help to separate the error-containing nucleic acid molecule from error-free nucleic acid molecules (see columns 14, lines 57-67 and column 15, lines 1-11) and MutH taught by Modrich *et al.*, and MutY taught by Makrigiorgos are used for the same purpose (ie., serving as a mismatch repair enzyme). One having ordinary skill in the art at the time the invention was made would have a reasonable expectation of success to cross-link the component (ie., MutH) to the error-containing nucleic acid molecule so that at least two components (ie., Mut H and the error containing nucleic acid molecule) are cross-linked to each other as recited in claims 16 and 17.

Conclusion

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

June 11, 2007

A handwritten signature in black ink, appearing to read 'Frank Lu', is positioned above the printed name.

FRANK LU
PRIMARY EXAMINER